EXHIBIT B

From: Leylah Drusbosky <ldrusbosky@guardanthealth.com>
Sent: Tuesday, March 9, 2021 11:57 AM
To: Kristin Price; Thereasa Rich
Cc: Lesli Kiedrowski
Subject: FW: [EXTERNAL] Natera's Commitment to MRD Testing
Attachments: 2021_ONC_Evidence_Review_Tumor_informed_vs.Tumor_naive_MRD.pdf

My Mayo FL group wants to discuss head to head May I ask for help prepping this meeting?
Thanks!
Ley

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From: "Starr, Jason S., D.O." <Starr.Jason@mayo.edu>
Date: Tuesday, March 9, 2021 at 12:52 PM
To: Leylah Drusbosky <ldrusbosky@guardanthealth.com>, "Jones, Jeremy C., M.D." <Jones.Jeremy1@mayo.edu>, "Mody, Kabir, M.D." <Mody.Kabir@mayo.edu>
Subject: FW: [EXTERNAL] Natera's Commitment to MRD Testing

Some talking points ☺

From: Natera, Inc. <reply@email.natera.com>
Sent: Tuesday, March 2, 2021 12:01 PM
To: Starr, Jason S., D.O. <Starr.Jason@mayo.edu>
Subject: [EXTERNAL] Natera's Commitment to MRD Testing

Dear Colleague,

Natera is committed to the science and precision of molecular residual disease (MRD) testing for improving patient care. We are proud that Signatera data has been published or presented from over 2,000 patients across 30+ tumor histologies. As this exciting field gains momentum, especially in early-stage CRC, there is concern about other laboratories rushing into the clinical MRD market and making potentially misleading claims with no peer-reviewed evidence , which may be detrimental to patients. As you review the evidence for any new MRD test, please keep in mind several minimum requirements for MRD product performance and clinical validation:

1. Does the test quantitate ctDNA, or does it only report ctDNA presence/absence? Quantitation is essential for monitoring tumor response during the patient's treatment.
2. What is the test performance and level of evidence in the intended use population, i.e. Stage II-III CRC? Performance in Stage IV CRC patients should be analyzed separately.

3. Has test performance been evaluated for the 3 critical decision points in early-stage CRC?
    - 30 days post-surgery to inform adjuvant treatment decisions.
    - Single test post adjuvant treatment.

- Serial surveillance testing, to rule in / rule out recurrence.

4. Is there sufficient evidence of test performance during adjuvant chemotherapy to enable clinical interpretation of a test result during treatment? Do patients achieve ctDNA clearance with adjuvant treatment (going from positive to negative)? To validate this, one must have serial samples from individual patients before, during, and after adjuvant chemotherapy.
5. In the surveillance setting, is the evidence sufficient to understand the false positive rate and negative predictive value (NPV) with serial sampling? Were serial blood samples analyzed for all patients, including non-relapsing patients?
6. What is the lead time from first MRD detection to radiographic recurrence? The more sensitive test will detect recurrence earlier, when the disease burden is lower.
7. Is there a breadth of evidence with consistent performance across multiple studies and tumor types?

For deeper insight into how Signatera's personalized, tumor-informed method measures up on these questions, particularly against tumor-naive methods, please see the enclosed material. We would be happy to schedule a conversation for a transparent review of our data.

Sincerely,

Natera, inc.

View Slides Here

* Natera, data on file

**Parikh, A. et. al. Minimal residual disease (MRD) detection in colorectal cancer (CRC) using a plasma- only integrated genomic and epigenomic ctDNA assay. ESMO 2020

The test described has been developed and its performance characteristics determined by the CLIA-certified laboratory performing the test. The test has not been cleared or approved by the US Food and Drug Administration (FDA). Although FDA is exercising enforcement discretion of premarket review and other regulations for laboratory-developed tests in the US, certification of the laboratory is required under CLIA to ensure the quality and validity of the tests. CAP accredited, ISO 13485 certified, and CLIA certified.

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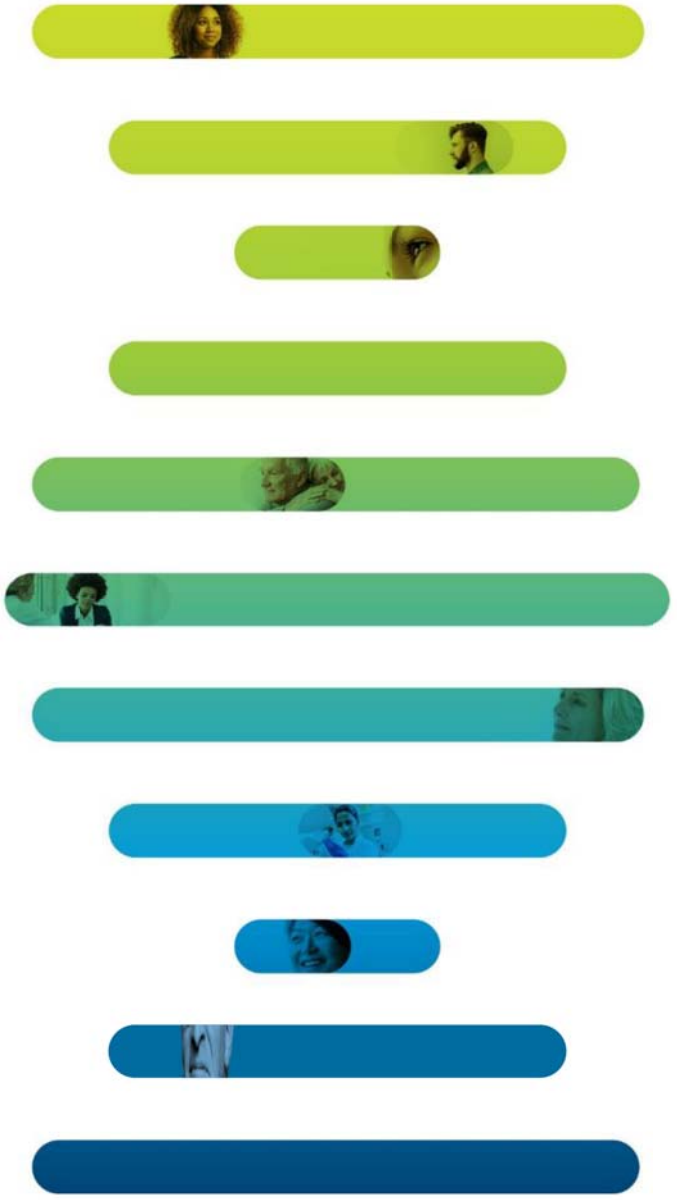
Evidence Review:

Tumor-informed vs. tumor-naïve MRD



March 2021

Evidence and performance matter

Weak evidence behind tumor-naïve methods

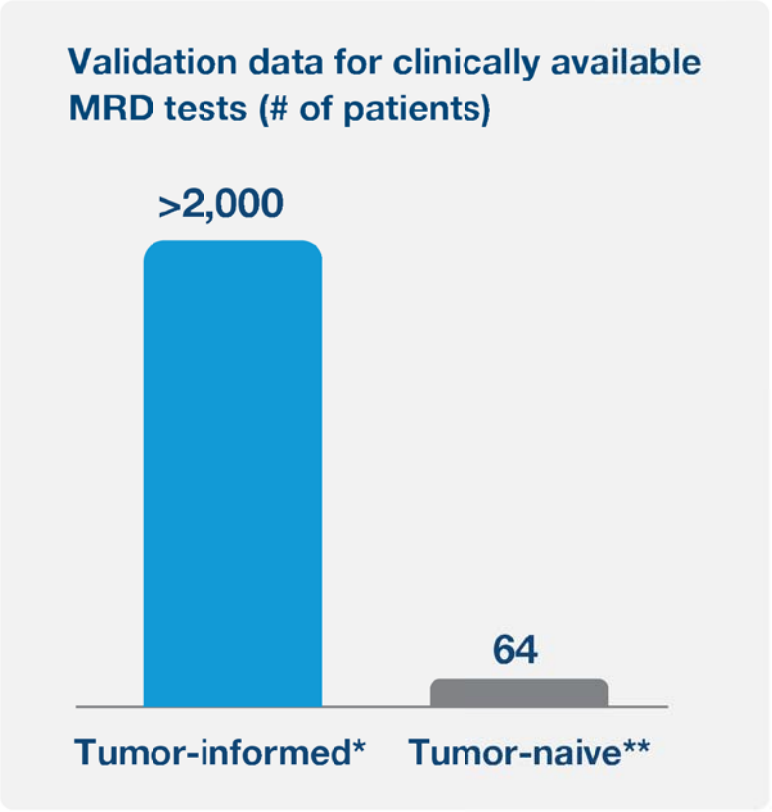
- No peer-reviewed data
- Significant gaps in study design and performance

Test performance with tumor-informed method is unsurpassed

- Hazard ratios, NPV/PPV, sensitivity/specificity
- Quantitation of disease burden
- Breadth and depth of evidence

Tumor-naïve data leaves unanswered questions

- No peer-reviewed evidence
- Small sample size (n=64)
- Unknown performance in the intended use population, e.g. Stage II-III. 19% of patients were Stage IV. No breakdown.
- Unknown performance at post-surgical timepoint, day 30
- Unknown how test performs during chemotherapy, and whether ctDNA clearance was observed in any patients
- Unknown lead times and FP rates in surveillance setting, with serial plasma only analyzed in patients who relapsed
- Unexplained statistical analysis and exclusion criteria:
  - Excluded patients with < 1 year of clinical followup
  - Exclusion of certain surveillance draws based on time from relapse
  - Disproportionate exclusion of patients from the surveillance analysis, who tested negative at earlier landmark timepoint



*Natera, data on file . **Parikh, A. et. a. Minimal residual disease (MRD) detection in colorectal cancer (CRC) using a plasma- only integrated genomic and epigenomic circulating tumor DNA (ctDNA) assay. ESMO 2020

Signatera data published or presented in > 2K patients

Author, Year	Journal/Congress	Tumor Type	Patients	Plasma
Abbosh et al., 2017	Nature	Lung	100	199
Correa et al., 2019	ESMO	RCC	45	81
Coombes et al., 2019	Clinical Cancer Research	Breast	49	215
Reinert et al., 2019	JAMA Oncol.	CRC	125	795
Christensen et al., 2019	JCO	Urothelial bladder carcinoma	68	656
Magbanua et al., 2020	AACR	Breast, neoadjuvant	84	291
Cohen et al., 2020	ESMO GI	CRC, oligo	93*	103
Kasi et al., 2020	ASCO	CRC, early and advanced	535	715
Loupakis et al., 2020	ESMO	CRC, oligo	113	192
Tarazona et al., 2020	ASCO	CRC	193**	1052
Ococks et al., 2020	ESMO	Esophageal adenocarcinoma	20	52
Hsu et al., 2020	ASCO	HCC, advanced	48	140
Bratman et al., 2020	Nature	IO (TNBC, melanoma, H&N, ovarian)	94	316
Powles et al., 2020	ESMO IO	Urothelial bladder carcinoma	581	1076
Henriksen et al., 2021	ASCO GI	CRC	260***	1503
Anandappa et al., 2021	ASCO GI	CRC	122	244
		Total	**>2,000 patient**	**>6,000 plasma**

* Subset analysis of patients from Kasi et al., ASCO poster 2020.
** Tarazona et al: Total cohort size 193 (125 of derived from Reinert cohort and 68 were unique cases)
***Henriksen et al: Total cohort size 260 (125 of derived from Reinert cohort and 135 were unique cases)

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Signatera relapse sensitivity 92% in the surveillance setting, based on multiple peer-reviewed studies

Cancer types in the adjuvant setting	Unique patients	Plasma samples	Key findings
NSCLC[1]	96 patients 14 relapses	210	93% sensitivity to relapse Average lead time 4.0 months
Bladder[2]	68 patients 16 relapses	651	100% sensitivity to relapse Average lead time 2.8 months
Colorectal[3]	130 patients 24 relapses	795	88% sensitivity to relapse Average lead time 8.7 months
Breast[4]	49 patients 18 relapses	208	89% sensitivity to relapse Average lead time 9.5 months
Total	**343 patients** **72 relapses**	**1864**	**Sensitivity overall 92%** **Specificity overall 99.7-99.8% per sample**

1. Abbosh C, Birkbak NJ, Wilson GA, et al. Phylogenetic ctDNA analysis depicts early-stage lung cancer evolution. *Nature*. 2017;545(7655):446-451.
2. Christensen E, Birkenkamp-Demtroder K, Sethi H, et al. Early Detection of Metastatic Relapse and Monitoring of Therapeutic Efficacy by Ultra-Deep Sequencing of Plasma Cell-Free DNA in Patients With Urothelial Bladder Carcinoma. *J Clin Oncol*. 2019;37(18):1547-1557.
3. Reinert T, Henriksen TV, Christensen E, et al. Analysis of plasma cell-free DNA by ultradeep sequencing in patients with stages I to III colorectal cancer. *JAMA Oncol*. 2019;5(8):1124–1131.
4. Coombes RC, Page K, Salari R, et al. Personalized detection of circulating tumor DNA antedates breast cancer metastatic recurrence *Clin Cancer Res*. 2019;;25(14):4255-426.

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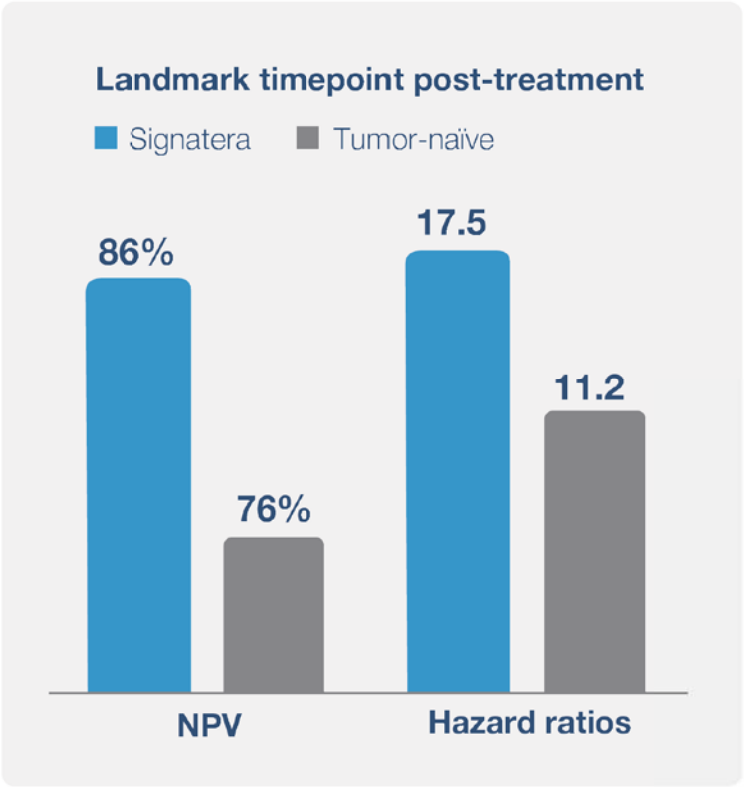
Three time points matter for performance assessment in CRC

	Signatera HR[1,3]	Tumor-naïve HR[2]
Single test 30 days post-surgery	7.2-14.0*	Unknown
Single test post-treatment	17.5	11.2
Serial testing in surveillance	43.5-47.5	Unknown

	Signatera NPV[1]	Tumor—naïve[2]
Single test 30 days post-surgery	88% (74/84)	Unknown
Single test post-treatment	86% (44/51)	76% (37/49)
Serial testing in surveillance	97% (58/60)	Unknown

***3/10 post-surgical positive patients cleared ctDNA with adjuvant chemotherapy and did not relapse, implying 70% PPV in patients who receive subsequent ACT**



1. Reinert T, Henriksen TV, Christensen E, et al. Analysis of plasma cell-free DNA by ultradeep sequencing in patients with stages I to III colorectal cancer. *JAMA Oncol.* 2019;5(8):1124–1131.
2. Parikh, A. et. al. Minimal residual disease (MRD) detection in colorectal cancer (CRC) using a plasma- only integrated genomic and epigenomic circulating tumor DNA (ctDNA) assay. ESMO 2020
3. Tarazona N, Henriksen T, Carbonell-Asins J, et al. Circulating tumor DNA to detect minimal residual disease, response to adjuvant therapy and identify patients at high risk of recurrence in stage I-III CRC. ASCO Poster. 2020

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Adjuvant treatment decisions depend on the post-surgical blood draw. Need data here.

Signatera NPV 88% at day 30, and PPV 98% without therapy*

***3/10 post-surgical positive patients cleared ctDNA with adjuvant chemotherapy and did not relapse, implying 70% PPV in patients who receive subsequent ACT**

1. Reinert T, Henriksen TV, Christensen E, et al. Analysis of plasma cell-free DNA by ultradeep sequencing in patients with stages I to III colorectal cancer. *JAMA Oncol.* 2019;5(8):1124–1131.
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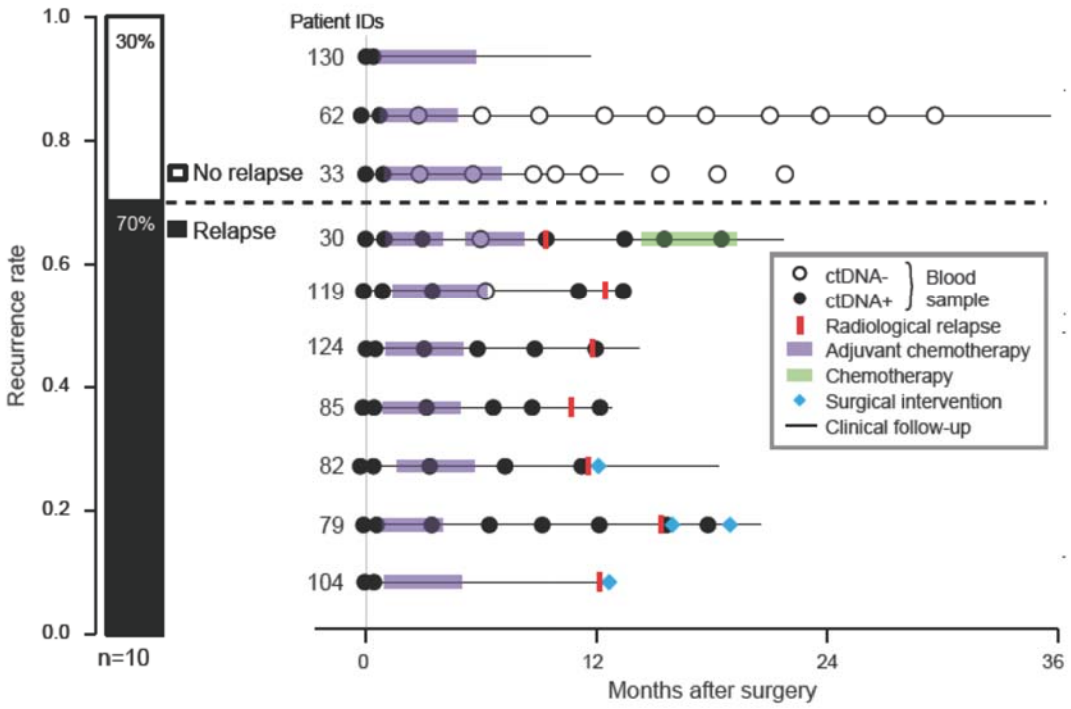
Signatera CRC validation showed persistent ctDNA clearance in 30% of patients, who tested positive pre-treatment



Must have serial data before, during and after adjuvant therapy

Must have evidence to interpret results during chemotherapy

Reinert T, Henriksen TV, Christensen E, et al. Analysis of plasma cell-free DNA by ultradeep sequencing in patients with stages I to III colorectal cancer. *JAMA Oncol.* 2019;5(8):1124–1131.

Surveillance validation should have serial sampling at regular intervals for all patients

For relapsing patients:

Need data on lead time for molecular relapse vs. radiographic relapse

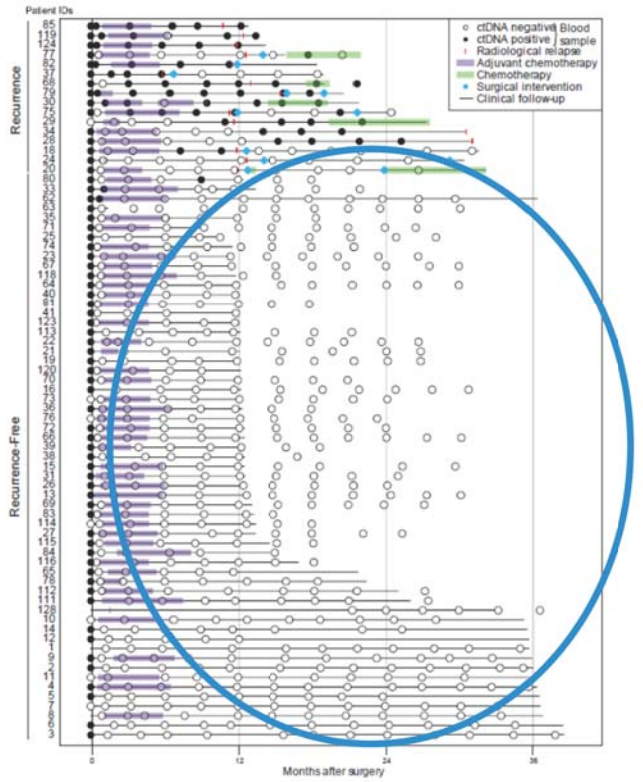
- 8.7 months avg lead time for Signatera

For non-relapsing patients:

Need serial data in order to establish true false positive rates and NPV/PPV

- 0.2% and 97%/98% for Signatera, respectively

eFigure 7. ctDNA Profiling Results From the 75 Patients Included in the Longitudinal Post-Definitive-Treatment ctDNA Analysis. Patients are ordered by recurrence status. Patients were considered positive if one or more plasma samples post-definitive-treatment was ctDNA-positive. Patient 80, which had a transient ctDNA-positive call at month 9 is likely false positive. From eFigure 3 it can be seen that only 2/16 mutations were called positive at month 9. All other post-operative samples from patient 80 were negative. In all other ctDNA-positive patients positivity persisted in the longitudinal samples and ctDNA status only changed to negative in case of clinical intervention.



Reinert T, Henriksen TV, Christensen E, et al. Analysis of plasma cell-free DNA by ultradeep sequencing in patients with stages I to III colorectal cancer. *JAMA Oncol.* 2019;5(8):1124–1131.

Results should be quantitative, for treatment monitoring

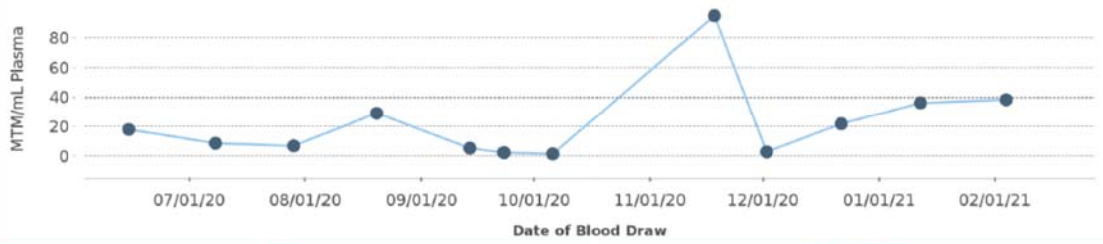
FINAL RESULTS SUMMARY

Signatera Positive

Date: 02/04/2021
MTM/mL: 38.43

Mean tumor molecules per mL is calculated based on the mean of ctDNA molecules detected per mL of the patient's plasma.

Historical Results



Date	MTM/mL
Sep 18, 2019	0.00
Dec 11, 2019	N/A
Jan 16, 2020	7.72
Apr 15, 2020	144.46
May 06, 2020	1.94
May 27, 2020	5.15
Jun 15, 2020	17.99
Jul 08, 2020	8.67
Jul 29, 2020	6.89
Aug 20, 2020	29.16

Tumor-naïve methods may have difficulty with quantitation, due to combination of genomic and epigenomic signatures

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Quantitative
Personalized
Tumor-informed
Validated in multiple studies
Covered by Medicare
Breakthrough designated by FDA

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